(n = 10), NHL (n = 7), Hodgkin's lymphoma (n = 6), advanced CML (n = 4), and advanced CLL (n = 4). 9 pts had previously undergone autografting. 80% received HLA-identical grafts. All pts were conditioned with fludarabine (30 mg/m^2/day, days -7 to -3), busulfan (0.8 mg/kg/dose IV × 8 doses) and rabbit ATG (2.5 mg/kg/day, days -4 to -2) followed by micro-dose methotrexate and tacrolimus. Stem cell source included peripheral blood (n = 26) or bone marrow (n = 4). All pts engrafted neutrophils and platelets promptly (median 15 and 16 days, respectively). There were no primary graft failures. Rates of grade II-IV and III-IV aGVHD were 43% (n = 13) and 23% (n = 7) respectively. 9 pts (30%) developed cGVHD but extensive cGVHD was seen in only 10% (n = 3). Day 100 TRM was 10% (n = 3). CMV and EBV reactivation occurred in 30% (n = 9) and 20% (n = 6) respectively. 2 pts developed PTLD requiring rituximab. 3 pts had BK-virus associated hemorrhagic cystitis. Chimerism analysis showed 100% donor CD33+ at all time points (days 30, 60, 100) and median donor CD3+ chimerism of 94% at day +30 and 100% at day +100. One pt had secondary graft failure. 23 pts (76%) were in CR after SCT. Kaplan-Meier estimates of overall survival (OS) and progression free survival (PFS) at 1 year are 62% and 43% respectively. OS (P = 0.95) and PFS (P = 0.65) was not statistically significant between recipients of matched and mismatched grafts. In conclusion, FBA and tacrolimus based GVHD prophylaxis achieved rapid donor chimerism and a favorably low incidence of TRM and cGVHD despite being tested in poor risk pts. However the rates of EBV reactivation and disease relapse warrant further exploration of this approach using lower doses of ATG (e.g. 5–6 mg/kg total dose).

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ALLOGENIC STEM CELL TRANSPLANTATION IN PATIENTS WITH ACQUIRED APLASTIC ANEMIA AND FANCONNI ANEMIA: A SINGLE CENTER EXPERIENCE OVER 11 YEARS

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We performed a retrospective analysis, of allogenic stem cell transplantation (allo-SCT) results, in 40 patients with diagnosis of acquired aplastic anemia or Fanconni Anemia, in a transplant center in Bogotá, Colombia, between 1996 and 2007.

During that period, 42 transplants were performed in 40 patients. 28 (70%) acquired aplastic anemia and 12 (30%) Fanconni's Anemia. 17 (42.5%) female/25 (62.5%) male. Mean age was 22 years (4–57).

Stem cells were obtained from peripheral blood in 36 (90%) and from bone marrow in 6 (15%). The majority of patients were of high risk; the mean time from diagnosis to transplant was 27.8 months (2–141) and 57.5% of them had received more than 20 transfusions before transplantation. Patients were conditioned with Cy-ATG in 24 (57.1%), high dose Cyclophosphamide (Cy) in 11 (26.2%), fludarabine-Cy-ATG in 3 (7.14%) and Alemtuzumab-Cy in 4 (9.52%).

Mean CD34+ cell dose was 3.3 (1.08–6.66), TNC: 9.7 (1.2–59.2).

Neutrophil engraftment was achieved at day +16 (3–54) post-transplantation.

At a mean follow up of 19.5 months (7–128), overall survival is 65%.

Comparison of results of different conditioning regimens shows that overall survival for patients conditioned with Cy alone is disappointing, 8/11 patients died, 6 due to GVHD and 2 due to infection. After adding ATG to Cy, mortality due to GVHD was significantly reduced. Only 7/24 patients died, GVHD was the cause of death only in 2. Infection was the cause of death in other 4. 2 patients had secondary graft failure, one died. The other received a second transplant and is alive with mixed chimerism, but free of transfusion support.

Of 4 patients treated with alemtuzumab containing regimens, 3 had secondary graft failure, 2 died, and one received a second transplant successfully.

On this group of patients Cy-ATG was the best conditioning regimen in terms of overall survival and GVHD incidence. The majority of patients in this cohort were remitted to transplant late in their disease, early treatment will probably improve the outcomes, as it has been confirmed in other papers.

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DOG LEUKOCYTE ANTIGEN (DLA)-IDENTICAL SIBLING CORD BLOOD TRANSPLANTATION (CBT) FOLLOWING MYELOABLATIVE TOTAL BODY IRRADIATION (TBI)

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Cord blood (CB) is increasingly used for hematopoietic cell transplantation due to its rapid availability and less stringent HLA matching requirements. However, low cell dose of CB units and delayed engraftment remain significant obstacles for increased use of CBT in adults. We aim to develop a large animal model of CBT by using outbred dogs to improve the understanding of engraftment across histocompatibility barriers and cell dose limitations of CBT. We harvested and cryopreserved individual units of canine CB obtained from litters following Caesarian section at day 54 to 60 of gestation. We asked if single or multiple units of DLA-identical sibling CB could engraft in DLA-identical recipient dogs. Eight adult dogs received 920 cGy TBI followed by intravenous infusion of thawed CB, either a single CB unit (n = 3) or multiple [2 to 4] CB units (n = 5) with a combined total nucleated cell (TNC) dose range 0.3–2.6 × 10^7/kg. Transplanted total CD34$^+$ cell dose was 0.2–2.5 × 10^5/kg. Postgrafting immunosuppression was cyclosporine + mycophenolate mofetil for 35 and 28 days, respectively. G-CSF was given until recovery of neutrophil counts. Three dogs died on days 13–17 due to neutropenic sepsis. Five dogs engrafted and survived; and are currently 265–621 days after CBT. Sustained neutrophil recovery >1000/μL occurred 29–35 days after CBT, and platelet recovery >20,000/μL was 38–84 days after CBT. Monthly chimerism analysis was assessed by PCR using informative microsatellite markers. Among each of the 4 surviving recipients of multiple unit CBT, all transplanted donor CB units contributed to hematopoiesis with sustained multi-donor chimerism. However, in all 4 dogs, 1 of the CB units eventually dominated hematopoiesis with sustained 75–95% donor chimerism. In all cases the dominant CB unit had the highest TNC dose. There was no acute or chronic GVHD. From 3–8 months after CBT, immune reconstitution studies normalized including T cell proliferation allo-stimulation index, 1^o and 2^o immune response to sheep red blood cells and recovery of the absolute number of CD4 and CD8 T-cell subsets. In summary, cryopreserved DLA-identical CB successfully engrafted and provided durable hematopoietic recovery. There was stable multi-donor chimerism and the CB unit with the greatest TNC dose predicted the dominant donor graft. The approximate minimum cell dose threshold for successful engraftment of a single CB unit with this conditioning regimen model was 0.8 × 10^7 TNC/kg.

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TACROLIMUS DOSING IN ALLOGENEIC HEMATOPOIETIC STEM-CELL TRANSPLANTATION RECIPIENTS RECEIVING VORICONAZOLE

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Tacrolimus (TAC) is primarily metabolized by the CYP450 3A4 isoenzyme. Voriconazole, often used to prevent fungal infections after allogeneic HSCT, is metabolized by the CYP450 3A4, 2C9 and 2C19 isosenzymes. Clinical trials in healthy volunteers have shown significant drug interactions between the two requiring TAC dose reduction. Ordinarily, TAC is started at the dose of 0.03 mg/kg IV daily on day -1. After starting it at this dose and having to reduce the dose substantially within 2–3 days in all patients receiving concomitant voriconazole 200 mg twice daily orally from day 0, we implemented a simple, preemptive TAC dose reduction strategy to maintain steady-state levels between 5 and 15 ng/mL. As a first step, IV TAC was initiated at the reduced dose of 0.022 mg/kg/day. As a second step, dose was reduced by 30–40% if the steady-state level 48 h after initiation of TAC (day +1) was between 7 and 10 ng/mL, and by 40–50% if the level was between 10 and 15 ng/mL. No change was made if the level was <7 ng/mL. Subsequently, levels were monitored 2–3 times a week and the dose